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FILE 'MEDLINE' ENTERED AT 09:33:33 ON 20 APR 2001

FILE 'CANCERLIT' ENTERED AT 09:33:33 ON 20 APR 2001

=> s (recombinant antibody fragments0

UNMATCHED LEFT PARENTHESIS '(RECOMBINAN'
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number of left parentheses.

=> s (recombinant antibody fragments)

L1 286 (RECOMBINANT ANTIBODY FRAGMENTS)

=> s l1 and multivalent?

L2 15 L1 AND MULTIVALENT?

=> d l2 1-15 all

L2 ANSWER 1 OF 15 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2001:157343 BIOSIS
DN PREV200100157343
TI Design and application of diabodies, triabodies and tetrabodies for cancer targeting.
AU Todorovska, Aneta; Roovers, Rob C.; Dolezal, Olan; Kortt, Alexander A.; Hoogenboom, Hennie R.; Hudson, Peter J. (1)
CS (1) CSIRO Health Science and Nutrition and CRC for Diagnostic Technologies, 343 Royal Parade, Parkville, VIC, 3052: peter.hudson@hsn.csiro.au Australia
SO Journal of Immunological Methods, (1 February, 2001) Vol. 248, No. 1-2, pp. 47-66. print.
ISSN: 0022-1759.
DT General Review
LA English
SL English
AB **Multivalent recombinant antibody fragments** provide high binding avidity and unique specificity to a wide range of target antigens and haptens. This review describes the design and expression of diabodies, triabodies and tetrabodies using examples of scFv molecules that target viruses (influenza neuraminidase) and cancer (Ep-CAM; epithelial cell adhesion molecule). We discuss the preferred choice of linker length between V-domains to direct the formation of either diabodies (60 kDa), triabodies (90 kDa) or tetrabodies (120 kDa), each with size, flexibility and valency suited to different applications for in vivo imaging and therapy. The increased binding valency of these scFv multimers results in high avidity (low off-rates). A particular advantage for tumour targeting is that molecules of 60-100 kDa have increased tumour penetration and fast clearance rates compared to the parent Ig (150 kDa). We highlight a number of cancer-targeting scFv multimers that have recently successfully undergone pre-clinical trials

IT Methods & Equipment
size exclusion chromatography: liquid chromatography
IT Miscellaneous Descriptors
antibody engineering technology; therapeutic antibody engineering; variable domain linker lengths

L2 ANSWER 2 OF 15 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2000:87930 BIOSIS
DN PREV200000087930
TI High avidity scFv multimers; Diabodies and triabodies.
AU Hudson, Peter J. (1); Kortt, Alexander A.
CS (1) CSIRO Molecular Science and CRC for Diagnostic Technologies, 343 Royal Parade, Parkville, VIC, 3052 Australia
SO Journal of Immunological Methods, (Dec. 10, 1999) Vol. 231, No. 1-2, pp. 177-189.
ISSN: 0022-1759.
DT General Review
LA English
SL English
AB **Multivalent recombinant antibody fragments** provide high binding avidity and unique specificity to a wide range of target antigens and haptens. This review describes how careful choice of linker length between V-domains creates new types of Fv modules with size, flexibility and valency suited to in vivo imaging and therapy. Further, we review the design of multi-specific Fv modules suited to cross-linking target antigens for cell-recruitment, viral delivery and immunodiagnostics. Single chain Fv antibody fragments (scFvs) are predominantly monomeric when the VH and VL domains are joined by polypeptide linkers of at least 12 residues. An scFv molecule with a linker of 3 to 12 residues cannot fold into a functional Fv domain and instead associates with a second scFv molecule to form a bivalent dimer (diabody, apprx 60 kDa). Reducing the linker length below three residues can force scFv association into trimers (triabodies, apprx 90 kDa) or tetramers (apprx 120 KDa) depending on linker length, composition and V-domain orientation. The increased binding valency in these scFv multimers results in high avidity (long off-rates). A particular advantage for tumor targeting is that molecules of apprx 60-100 kDa have increased tumor penetration and fast clearance rates compared to the parent Ig. A number of cancer-targeting scFv multimers have recently undergone pre-clinical evaluation for in vivo stability and efficacy. Bi- and tri-specific multimers can be formed by association of different scFv molecules and, in the first examples, have been designed as cross-linking reagents for T-cell recruitment into tumors (immunotherapy) and as red blood cell agglutination reagents (immunodiagnostics).
CC Biochemical Studies - General *10060
Biochemical Methods - General *10050
Neoplasms and Neoplastic Agents - General *24002
Immunology and Immunochemistry - General; Methods *34502
IT Major Concepts
Biochemistry and Molecular Biophysics; Immune System (Chemical Coordination and Homeostasis)
IT Parts, Structures, & Systems of Organisms
T cells: blood and lymphatics, immune system; red blood cells: blood and lymphatics
IT Chemicals & Biochemicals
Ig [immunoglobulin]; antigens; diabodies; haptens; high avidity scFv multimers; **multivalent recombinant antibody fragments**; triabodies
IT Methods & Equipment
electron microscopy: methodological approach, microscopy method, microscopy: CB
IT Miscellaneous Descriptors
amino acid sequence; protein flexibility; protein size; protein valency; tumor targeting

L2 ANSWER 3 OF 15 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1997:367125 BIOSIS
DN PREV199799659058
TI New protein engineering approaches to **multivalent** and bispecific antibody fragments.
AU Pluckthun, Andreas (1); Pack, Peter
CS (1) Biochemisches Inst. Univ. Zuerich, Winterthurestr. 190, CH-8057 Zurich

clinical studies now available for suitably engineered fragments. We foresee therapeutic advances from a modular, systematic approach to optimizing pharmacokinetics, stability and functional affinity, which should prove possible with the new recombinant molecular designs.

CC Biochemical Methods - Proteins, Peptides and Amino Acids *10054
Replication, Transcription, Translation *10300
Physiology and Biochemistry of Bacteria *31000
Microbiological Apparatus, Methods and Media *32000
Immunology and Immunochemistry - General; Methods *34502

BC Enterobacteriaceae *06702

IT Major Concepts
Immune System (Chemical Coordination and Homeostasis); Methods and Techniques; Molecular Genetics (Biochemistry and Molecular Biophysics); Physiology

IT Miscellaneous Descriptors
ANTIBODY FRAGMENTS; BIOMEDICAL ENGINEERING; BISPECIFIC; EXPRESSION TECHNOLOGY; IMMUNE SYSTEM; IMMUNOLOGICAL ENGINEERING; MINIANTIBODIES; MULTIVALENCY; **MULTIVALENT**; PROTEIN ENGINEERING; RECOMBINANT MOLECULAR DESIGNS

ORGN Super Taxa
Enterobacteriaceae: Eubacteria, Bacteria

ORGN Organism Name
Escherichia coli (Enterobacteriaceae)

ORGN Organism Superterms
bacteria; eubacteria; microorganisms

L2 ANSWER 4 OF 15 BIOSIS COPYRIGHT 2001 BIOSIS

AN 1995:125578 BIOSIS

DN PREV199598139878

TI Single-chain Fvs.

AU Raag, Reetta; Whitlow, Marc (1)

CS (1) Protein Biophysics, Berlex Biosci., 15049 San Pablo Ave., P.O. Box 4099, Richmond, CA 94804 USA

SO FASEB Journal, (1995) Vol. 9, No. 1, pp. 73-80.
ISSN: 0892-6638.

DT Article

LA English

AB Single-chain Fvs (sFvs) are **recombinant antibody fragments** consisting of only the variable light chain (VL) and variable heavy chain (VH) domains covalently connected to one another by a polypeptide linker. Due to their small size, sFvs have rapid pharmacokinetics and tumor penetration in vivo. Single-chain Fvs also show a concentration-dependent tendency to oligomerize. Bivalent sFvs are formed when the variable domains of a sFv disassociate from one another and reassociate with the variable domains of a second sFv. Similar rearrangement and reassociation of variable domains from different sFvs can result in the formation of trimers or higher multimeric oligomers. Each Fv in a bivalent or **multivalent** Fv is composed of the V-L domain from one sFv and the V-H domain from a second sFv. Modifying linker length or the inclusion of antigen may stabilize the V-L/V-H interface against rearrangement such that specific multimeric or monomeric forms of sFvs may be isolated. Nuclear magnetic resonance studies have shown that McPC603-derived Fv and sFvs have similar structures, and that the sFv linker is a rapidly moving, highly flexible peptide with a random coil-like structure. In X-ray crystallographic investigations of three different sFvs, linkers have also been found to be disordered. Indirect evidence suggests that a monomeric sFv has been crystallized in one case, and dimeric sFvs in the other two.

CC Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biophysics - Molecular Properties and Macromolecules *10506
Immunology and Immunochemistry - General; Methods *34502

BC Vertebrata - Unspecified *85150

IT Major Concepts
Biochemistry and Molecular Biophysics; Immune System (Chemical Coordination and Homeostasis)

IT Miscellaneous Descriptors
AGGREGATION; NMR; RECOMBINANT ANTIBODY FRAGMENT; STRUCTURE; X-RAY CRYSTALLOGRAPHY

ORGN Super Taxa
Vertebrata - Unspecified: Vertebrata, Chordata, Animalia

ORGN Organism Name
Vertebrata (Vertebrata - Unspecified)

· **fragments** provide high binding avidity and unique specificity to a wide range of target antigens and haptens. This review describes the design and expression of diabodies, triabodies and tetrabodies using examples of scFv mols. that target viruses (influenza neuraminidase) and cancer (Ep-CAM; epithelial cell adhesion mol.). We discuss the preferred choice of linker length between V-domains to direct the formation of either diabodies (60 kDa), triabodies (90 kDa) or tetrabodies (120 kDa), each with size, flexibility and valency suited to different applications for in vivo imaging and therapy. The increased binding valency of these scFv multimers results in high avidity (low off-rates). A particular advantage for tumor targeting is that mols. of 60-100 kDa have increased tumor penetration and fast clearance rates compared to the parent Ig (150 kDa). We highlight a no. of cancer-targeting scFv multimers that have recently successfully undergone pre-clin. trials for in vivo stability and efficacy. We also review the design of multi-specific Fv modules suited to cross-link two or more different target antigens. These bi- and tri-specific multimers can be formed by assocn. of different scFv mols. and, in the first examples, have been designed as crosslinking reagents for T-cell recruitment into tumors (immunotherapy), viral retargeting (gene therapy) and as red blood cell agglutination reagents (immunodiagnostics).

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L2 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2001 ACS
AN 2000:60685 CAPLUS
DN 132:235560
TI High avidity scFv multimers; diabodies and triabodies
AU Hudson, P. J.; Kortt, A. A.
CS CSIRO Molecular Science and CRC for Diagnostic Technologies, Victoria, 3052, Australia
SO J. Immunol. Methods (1999), 231(1-2), 177-189
CODEN: JIMMBG; ISSN: 0022-1759
PB Elsevier Science B.V.
DT Journal; General Review
LA English
CC 15-0 (Immunochemistry)
Section cross-reference(s): 8
AB **Multivalent recombinant antibody fragments** provide high binding avidity and unique specificity to a wide range of target antigens and haptens. This review, with 67 refs., describes how careful choice of linker length between V-domains creates new types of Fv modules with size, flexibility and valency suited to in vivo imaging and therapy. Further, the authors review the design of multi-specific Fv modules suited to crosslinking target antigens for cell-recruitment, viral delivery and immunodiagnostics. Single chain Fv antibody fragments (scFvs) are predominantly monomeric when the VH and VL domains are joined by polypeptide linkers of at least 12 residues. An scFv mol. with a linker of 3 to 12 residues cannot fold into a functional Fv domain and instead assocs. with a second scFv mol. to form a bivalent dimer (diabody, .apprx.60 kDa). Reducing the linker length below three residues can force scFv assocn. into trimers (triabodies, .apprx.90 kDa) or tetramers (.apprx.120 KDa) depending on linker length, compn. and V-domain orientation. The increased binding valency in these scFv multimers results in high avidity (long off-rates). A particular advantage for tumor targeting is that mols. of .apprx.60-100 kDa have increased tumor penetration and fast clearance rates compared to the parent Ig. A no. of cancer-targeting scFv multimers have recently undergone pre-clin. evaluation for in vivo stability and efficacy. Bi- and tri-specific multimers can be formed by assocn. of different scFv mols. and, in the first examples, have been designed as crosslinking reagents for T-cell recruitment into tumors (immunotherapy) and as red blood cell agglutination reagents (immunodiagnostics).
ST review single chain antibody multimer
IT Antitumor agents
(high avidity single-chain antibody multimers in relation to)
IT Diagnosis
(immunodiagnosis; high avidity single-chain antibody multimers in relation to)
IT Antibodies
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic

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L2 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2001 ACS
AN 1997:520511 CAPLUS
DN 127:204030
TI New protein engineering approaches to **multivalent** and bispecific antibody fragments
AU Pluckthun, Andreas; Pack, Peter
CS Biochemisches Institut der Universitat Zurich, Zurich, CH-8057, Switz.
SO Immunotechnology (1997), 3(2), 83-105
CODEN: IOTEER; ISSN: 1380-2933
PB Elsevier
DT Journal; General Review
LA English
CC 15-0 (Immunochemistry)
AB A review with 174 refs. Multivalency is one of the hallmarks of

ST review bispecific antibody engineering; scFv antibody engineering review
IT Antibodies
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); PRP (Properties); BIOL (Biological study); PREP (Preparation)
(bispecific; protein engineering of **multivalent** and bispecific antibody fragments)
IT Antibodies
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); PRP (Properties); BIOL (Biological study); PREP (Preparation)
(mini-; protein engineering of **multivalent** and bispecific antibody fragments)
IT Escherichia coli
(protein engineering of **multivalent** and bispecific antibody fragments)
IT Immunoglobulin fragments
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); PRP (Properties); BIOL (Biological study); PREP (Preparation)
(protein engineering of **multivalent** and bispecific antibody fragments)
IT Single chain antibodies
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); PRP (Properties); BIOL (Biological study); PREP (Preparation)
(scFv; protein engineering of **multivalent** and bispecific antibody fragments)
IT Protein motifs
(self-assocg.; protein engineering of **multivalent** and bispecific antibody fragments)

L2 ANSWER 8 OF 15 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN 2001075273 EMBASE
TI Design and application of diabodies, triabodies and tetrabodies for cancer targeting.
AU Todorovska A.; Roovers R.C.; Dolezal O.; Kortt A.A.; Hoogenboom H.R.; Hudson P.J.
CS P.J. Hudson, CSIRO Health Science and Nutrition, CRC for Diagnostic Technologies, 343 Royal Parade, Parkville, Vic. 3052, Australia. peter.hudson@hsn.csiro.au
SO Journal of Immunological Methods, (1 Feb 2001) 248/1-2 (47-66).
Refs: 92
ISSN: 0022-1759 CODEN: JIMMBG
PUI S 0022-1759(00)00342-2
CY Netherlands
DT Journal; General Review
FS 016 Cancer
026 Immunology, Serology and Transplantation
LA English
SL English
AB **Multivalent recombinant antibody fragments** provide high binding avidity and unique specificity to a wide range of target antigens and haptens. This review describes the design and expression of diabodies, triabodies and tetrabodies using examples of scFv molecules that target viruses (influenza neuraminidase) and cancer (Ep-CAM; epithelial cell adhesion molecule). We discuss the preferred choice of linker length between V-domains to direct the formation of either diabodies (60 kDa), triabodies (90 kDa) or tetrabodies (120 kDa), each with size, flexibility and valency suited to different applications for in vivo imaging and therapy. The increased binding valency of these scFv multimers results in high avidity (low off-rates). A particular advantage for tumour targeting is that molecules of 60-100 kDa have increased tumour penetration and fast clearance rates compared to the parent Ig (150 kDa). We highlight a number of cancer-targeting scFv multimers that have recently successfully undergone pre-clinical trials for in vivo stability and efficacy. We also review the design of multi-specific Fv modules suited to cross-link two or more different target antigens. These bi- and tri-specific multimers can be formed by association of different scFv molecules and, in the first examples, have been designed as cross-linking reagents for T-cell recruitment into tumours (immunotherapy), viral retargeting (gene therapy) and as red blood cell agglutination reagents (immunodiagnostics). .COPYRGT. 2001 Elsevier

human cell
review
priority journal
Drug Descriptors:
*antibody
*moc 31 antibody
single chain fv antibody
immunoglobulin
polymer
dimer
cell adhesion molecule
tetramer
monomer
unclassified drug
RN (immunoglobulin) 9007-83-4

L2 ANSWER 9 OF 15 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN 2000213172 EMBASE
TI High avidity scFv multimers; diabodies and triabodies.
AU Hudson P.J.; Kortt A.A.
CS P.J. Hudson, CSIRO Molecular Science, CRC for Diagnostic Technologies, 343 Royal Parade, Parkville, Vic. 3052, Australia.
peter.hudson@molsci.csiro.au
SO Journal of Immunological Methods, (1999) 231/1-2 (177-189).
Refs: 67
ISSN: 0022-1759 CODEN: JIMMBG
PUI S 0022-1759(99)00157-X
CY Netherlands
DT Journal; Article
FS 026 Immunology, Serology and Transplantation
LA English
SL English
AB **Multivalent recombinant antibody fragments** provide high binding avidity and unique specificity to a wide range of target antigens and haptens. This review describes how careful choice of linker length between V-domains creates new types of Fv modules with size, flexibility and valency suited to in vivo imaging and therapy. Further, we review the design of multi-specific Fv modules suited to cross-linking target antigens for cell-recruitment, viral delivery and immunodiagnostics. Single chain Fv antibody fragments (scFvs) are predominantly monomeric when the V(H) and V(L) domains are joined by polypeptide linkers of at least 12 residues. An scFv molecule with a linker of 3 to 12 residues cannot fold into a functional Fv domain and instead associates with a second scFv molecule to form a bivalent dimer (diabody, .apprx. 60 kDa). Reducing the linker length below three residues can force scFv association into trimers (triabodies, .apprx. 90 kDa) or tetramers (.apprx. 120 KDa) depending on linker length, composition and V-domain orientation. The increased binding valency in these scFv multimers results in high avidity (long off-rates). A particular advantage for tumor targeting is that molecules of .apprx. 60-100 kDa have increased tumor penetration and fast clearance rates compared to the parent Ig. A number of cancer-targeting scFv multimers have recently undergone pre-clinical evaluation for in vivo stability and efficacy. Bi- and tri-specific multimers can be formed by association of different scFv molecules and, in the first examples, have been designed as cross-linking reagents for T-cell recruitment into tumors (immunotherapy) and as red blood cell agglutination reagents (immunodiagnostics). (C) 1999 Elsevier Science B.V.
CT Medical Descriptors:
*binding affinity
*immunoglobulin variable region
antibody specificity
cross linking
T lymphocyte
serodiagnosis
article
priority journal
Drug Descriptors:
*recombinant antibody
*immunoglobulin light chain
*immunoglobulin heavy chain
hapten

SL English
AB Multivalency is one of the hallmarks of antibodies, by which enormous gains in functional affinity, and thereby improved performance in vivo and in a variety of in vitro assays are achieved. Improved in vivo targeting and more selective localization are another consequence of multivalency. We summarize recent progress in engineering multivalency from **recombinant antibody fragments** by using miniantibodies (scFv fragments linked with hinges and oligomerization domains), spontaneous scFv dimers with short linkers (diabodies), or chemically crosslinked antibody fragments. Directly related to this are efforts of bringing different binding sites together to create bispecific antibodies. For this purpose, chemically linked fragments, diabodies, scFv-scFv tandems and bispecific miniantibodies have been investigated. Progress in E. coli expression technology makes the amounts necessary for clinical studies now available for suitably engineered fragments. We foresee therapeutic advances from a modular, systematic approach to optimizing pharmacokinetics, stability and functional affinity, which should prove possible with the new recombinant molecular designs.
CT Medical Descriptors:
*genetic engineering
antibody specificity
antibody structure
binding site
biotechnology
cross linking
escherichia coli
immunoassay
nonhuman
oligomerization
priority journal
protein domain
review
Drug Descriptors:
*bispecific antibody
recombinant protein

L2 ANSWER 11 OF 15 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN 95034346 EMBASE
DN 1995034346
TI Single-chain Fvs.
AU Raag R.; Whitlow M.
CS Protein Biophysics, Berlex Biosciences, 15049 San Pablo Ave.,Richmond, CA 94804, United States
SO FASEB Journal, (1995) 9/1 (73-80).
ISSN: 0892-6638 CODEN: FAJOEC
CY United States
DT Journal; General Review
FS 029 Clinical Biochemistry
LA English
SL English
AB Single-chain Fvs (sFvs) are **recombinant antibody fragments** consisting of only the variable light chain (V(L)) and variable heavy chain (V(H)) domains covalently connected to one another by a polypeptide linker. Due to their small size, sFvs have rapid pharmacokinetics and tumor penetration in vivo. Single-chain Fvs also show a concentration-dependent tendency to oligomerize. Bivalent sFvs are formed when the variable domains of a sFv disassociate from one another and reassociate with the variable domains of a second sFv. Similar rearrangement and reassociation of variable domains from different sFvs can result in the formation of trimers or higher multimeric oligomers. Each Fv in a bivalent or **multivalent** Fv is composed of the Vi domain from one sFv and the VH domain from a second sFv. Modifying linker length or the inclusion of antigen may stabilize the V(L)/V(H) interface against rearrangement such that specific multimeric or monomeric forms of sFvs may be isolated. Nuclear magnetic resonance studies have shown that McPC603-derived Fv and sFvs have similar structures, and that the sFv linker is a rapidly moving, highly flexible peptide with a random coil-like structure. In X-ray crystallographic investigations of three different sFvs, linkers have also been found to be disordered. Indirect evidence suggests that a monomeric sFv has been crystallized in one case, and dimeric sFvs in the other two.
CT Medical Descriptors:
*protein stability

TI Design and application of diabodies, triabodies and tetrabodies for cancer targeting.
AU Todorovska A; Roovers R C; Dolezal O; Kortt A A; Hoogenboom H R; Hudson P J
CS CSIRO Health Science and Nutrition and CRC for Diagnostic Technologies, 343 Royal Parade, Victoria 3052, Parkville, Australia.
SO JOURNAL OF IMMUNOLOGICAL METHODS, (2001 Feb 1) 248 (1-2) 47-66. Ref: 92
Journal code: IFE. ISSN: 0022-1759.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200104
AB **Multivalent recombinant antibody fragments** provide high binding avidity and unique specificity to a wide range of target antigens and haptens. This review describes the design and expression of diabodies, triabodies and tetrabodies using examples of scFv molecules that target viruses (influenza neuraminidase) and cancer (Ep-CAM; epithelial cell adhesion molecule). We discuss the preferred choice of linker length between V-domains to direct the formation of either diabodies (60 kDa), triabodies (90 kDa) or tetrabodies (120 kDa), each with size, flexibility and valency suited to different applications for in vivo imaging and therapy. The increased binding valency of these scFv multimers results in high avidity (low off-rates). A particular advantage for tumour targeting is that molecules of 60-100 kDa have increased tumour penetration and fast clearance rates compared to the parent Ig (150 kDa). We highlight a number of cancer-targeting scFv multimers that have recently successfully undergone pre-clinical trials for in vivo stability and efficacy. We also review the design of multi-specific Fv modules suited to cross-link two or more different target antigens. These bi- and tri-specific multimers can be formed by association of different scFv molecules and, in the first examples, have been designed as cross-linking reagents for T-cell recruitment into tumours (immunotherapy), viral retargeting (gene therapy) and as red blood cell agglutination reagents (immunodiagnostics).
CT Check Tags: Animal; Human
Amino Acid Sequence
Antibodies, Bispecific: CH, chemistry
Antibodies, Bispecific: GE, genetics
*Antibodies, Bispecific: TU, therapeutic use
Antibody Affinity
Dimerization
Immunoglobulin Fragments: CH, chemistry
Immunoglobulin Fragments: GE, genetics
*Immunoglobulin Fragments: TU, therapeutic use
Molecular Sequence Data
*Neoplasms: TH, therapy
*Protein Engineering
CN 0 (Antibodies, Bispecific); 0 (Immunoglobulin Fragments); 0 (immunoglobulin Fv)

L2 ANSWER 13 OF 15 MEDLINE
AN 2000115639 MEDLINE
DN 20115639
TI High avidity scFv multimers; diabodies and triabodies.
AU Hudson P J; Kortt A A
CS CSIRO Molecular Science and CRC for Diagnostic Technologies, 343 Royal Parade, Parkville, Victoria, 3052, Australia..
peter.hudson@molsci.csiro.au
SO JOURNAL OF IMMUNOLOGICAL METHODS, (1999 Dec 10) 231 (1-2) 177-89. Ref: 67
Journal code: IFE. ISSN: 0022-1759.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals; Cancer Journals
EM 200005
EW 20000501
AB **Multivalent recombinant antibody fragments** provide high binding avidity and unique specificity to a

clearance rates compared to the parent Ig. A number of cancer-targeting scFv multimers have recently undergone pre-clinical evaluation for in vivo stability and efficacy. Bi- and tri-specific multimers can be formed by association of different scFv molecules and, in the first examples, have been designed as cross-linking reagents for T-cell recruitment into tumors (immunotherapy) and as red blood cell agglutination reagents (immunodiagnostics).

CT Check Tags: Animal; Human
*Antibody Affinity: IM, immunology
Gene Expression
Immunoglobulin Fragments: BI, biosynthesis
Immunoglobulin Fragments: CH, chemistry
Immunoglobulin Fragments: GE, genetics
*Immunoglobulin Fragments: IM, immunology
Immunoglobulin Variable Region: BI, biosynthesis
Immunoglobulin Variable Region: GE, genetics
Immunoglobulin Variable Region: IM, immunology
Recombinant Fusion Proteins: BI, biosynthesis
Recombinant Fusion Proteins: GE, genetics
Recombinant Fusion Proteins: IM, immunology

CN 0 (Immunoglobulin Fragments); 0 (Immunoglobulin Variable Region); 0 (Recombinant Fusion Proteins)

L2 ANSWER 14 OF 15 MEDLINE
AN 97380304 MEDLINE
DN 97380304
TI New protein engineering approaches to **multivalent** and bispecific antibody fragments.
AU Pluckthun A; Pack P
CS Biochemisches Institut der Universitat Zurich, Switzerland.
SO IMMUNOTECHNOLOGY, (1997 Jun) 3 (2) 83-105. Ref: 174
Journal code: CR0. ISSN: 1380-2933.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199711
EW 19971101
AB Multivalency is one of the hallmarks of antibodies, by which enormous gains in functional affinity, and thereby improved performance in vivo and in a variety of in vitro assays are achieved. Improved in vivo targeting and more selective localization are another consequence of multivalency. We summarize recent progress in engineering multivalency from **recombinant antibody fragments** by using miniantibodies (scFv fragments linked with hinges and oligomerization domains), spontaneous scFv dimers with short linkers (diabodies), or chemically crosslinked antibody fragments. Directly related to this are efforts of bringing different binding sites together to create bispecific antibodies. For this purpose, chemically linked fragments, diabodies, scFv-scFv tandems and bispecific miniantibodies have been investigated. Progress in E. coli expression technology makes the amounts necessary for clinical studies now available for suitably engineered fragments. We foresee therapeutic advances from a modular, systematic approach to optimizing pharmacokinetics, stability and functional affinity, which should prove possible with the new recombinant molecular designs.
CT Check Tags: Animal; Human
Amino Acid Sequence
*Antibodies, Bispecific: CH, chemistry
Antibodies, Bispecific: GE, genetics
*Immunoglobulin Fragments: CH, chemistry
Immunoglobulin Fragments: GE, genetics
Molecular Sequence Data
*Protein Engineering
Recombinant Proteins: CH, chemistry
CN 0 (Antibodies, Bispecific); 0 (Immunoglobulin Fragments); 0 (Recombinant Proteins)

L2 ANSWER 15 OF 15 MEDLINE
AN 95121810 MEDLINE
DN 95121810
TI Single-chain Fvs.

formed when the variable domains of a sFv disassociate from one another and reassociate with the variable domains of a second sFv. Similar rearrangement and reassociation of variable domains from different sFvs can result in the formation of trimers or higher multimeric oligomers. Each Fv in a bivalent or **multivalent** Fv is composed of the VL domain from one sFv and the VH domain from a second sFv. Modifying linker length or the inclusion of antigen may stabilize the VL/VH interface against rearrangement such that specific multimeric or monomeric forms of sFvs may be isolated. Nuclear magnetic resonance studies have shown that McPC603-derived Fv and sFvs have similar structures, and that the sFv linker is a rapidly moving, highly flexible peptide with a random coil-like structure. In X-ray crystallographic investigations of three different sFvs, linkers have also been found to be disordered. Indirect evidence suggests that a monomeric sFv has been crystallized in one case, and dimeric sFvs in the other two.

CT Check Tags: Human
Amino Acid Sequence
Crystallization
*Immunoglobulin Fragments: CH, chemistry
Immunoglobulin Fragments: ME, metabolism
*Immunoglobulin Variable Region: CH, chemistry
Immunoglobulin Variable Region: ME, metabolism
Macromolecular Systems
Molecular Sequence Data
Nuclear Magnetic Resonance
Recombinant Proteins: CH, chemistry
Recombinant Proteins: ME, metabolism

CN 0 (immunoglobulin Fv); 0 (Immunoglobulin Fragments); 0 (Immunoglobulin Variable Region); 0 (Macromolecular Systems); 0 (Recombinant Proteins)

TERMINAL (ENTER 1, 2, 3, OR ?):2

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NEWS 4	Oct 27	SET ABBREVIATIONS and SET PLURALS extended in Derwent World Patents Index files
NEWS 5	Oct 27	Patent Assignee Code Dictionary now available in Derwent Patent Files
NEWS 6	Oct 27	Plasdoc Key Serials Dictionary and Echoing added to Derwent Subscriber Files WPIDS and WPIX
NEWS 7	Nov 29	Derwent announces further increase in updates for DWPI
NEWS 8	Dec 5	French Multi-Disciplinary Database PASCAL Now on STN
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NEWS 12	Dec 17	Corrosion Abstracts on STN
NEWS 13	Dec 17	SYNTHLINE from Prous Science now available on STN
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NEWS 15	Jan 05	AIDSLINE is being removed from STN
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NEWS 17	Feb 16	TOXLINE no longer being updated

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FILE 'HOME' ENTERED AT 15:37:41 ON 19 APR 2001

=> file biosis caplus embase medline cancerlit

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FILE 'BIOSIS' ENTERED AT 15:37:57 ON 19 APR 2001

FILE 'CAPLUS' ENTERED AT 15:37:57 ON 19 APR 2001

FILE 'EMBASE' ENTERED AT 15:37:57 ON 19 APR 2001

FILE 'MEDLINE' ENTERED AT 15:37:57 ON 19 APR 2001

FILE 'CANCERLIT' ENTERED AT 15:37:57 ON 19 APR 2001

=> l (dual antigen binding site)

L5 0 L4 AND DIMER

=> s l4 and dimer?

L6 1 L4 AND DIMER?

=> d l6 1 all

L6 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2001 ACS
AN 1995:796621 CAPLUS
DN 123:196269
TI Multiple regions of human Fc.gamma.RII (CD32) contribute to the binding of IgG
AU Hulett, Mark D.; Witort, Ewa; Brinkworth, Ross I.; McKenzie, Ian F. C.; Hogarth, P. Mark
CS Austin Res. Inst., Austin Hosp., Victoria, 3082, Australia
SO J. Biol. Chem. (1995), 270(36), 21188-94
CODEN: JBCHA3; ISSN: 0021-9258
DT Journal
LA English
CC 15-3 (Immunochemistry)
AB The low affinity receptor for IgG, Fc.gamma.RII (CD32), has a wide distribution on hematopoietic cells where it is responsible for a diverse range of cellular responses crucial for immune regulation and resistance to infection. Fc.gamma.RII is a member of the Ig superfamily, contg. an extracellular region of two Ig-like domains. The IgG binding site of human Fc.gamma.RII has been localized to an 8-amino acid segment of the second extracellular domain, Asn154-Ser161. In this study, evidence is presented to suggest that domain 1 and two addnl. regions of domain 2 also contribute to the binding of IgG by Fc.gamma.RII. Chimeric receptors **generated** by exchanging the extracellular domains and segments of domain 2 between Fc.gamma.RII and the structurally related Fc.epsilon.RI .alpha. chain were used to demonstrate that substitution of domain 1 in its entirety or the domain 2 regions encompassing residues Ser109-Val116 and Ser130-Thr135 resulted in a loss of the ability of these receptors to bind hIgG1 in **dimeric** form. Site-directed mutagenesis performed on individual residues within and flanking the Ser109-Val116 and Ser130-Thr135 domain 2 segments indicated that substitution of Lys113, Pro114, Leu115, Val116, Phe129, and His131 profoundly decreased the binding of hIgG1, whereas substitution of Asp133 and Pro134 increased binding. These findings suggest that not only is domain 1 contributing to the affinity of IgG binding by Fc.gamma.RII but, importantly, that the domain 2 regions Ser109-Val116 and Phe1219-Thr135 also play key roles in the binding to hIgG1. The location of these binding regions on a mol. model of the entire extracellular region of Fc.gamma.RII indicates that they comprise loops that are **juxtaposed** in domain 2 at the interface with domain 1, with the putative crucial binding residues forming a hydrophobic pocket surrounded by a wall of predominantly arom. and basic residues.
ST FcgammaRII receptor structure ligand binding; CD32 **antigen** structure ligand binding; IgG receptor structure function
IT Immune complexes
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(human Fc.gamma.RII receptor structure in binding of)
IT Molecular modeling
(of human Fc.gamma.RII receptor)
IT Immunoglobulin receptors
Receptors
RL: BPR (Biological process); PRP (Properties); BIOL (Biological study); PROC (Process)
(Fc.gamma.RIIA (IgG fragment Fc receptor IIA), human; domain structure in ligand binding by)
IT Molecular structure-biological activity relationship
(ligand-binding, of human Fc.gamma.RII receptor)
IT 56-41-7, Alanine, biological studies
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(residue 133 or 134; enhanced ligand binding by human Fc.gamma.RII receptor on substitution with)

The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s polymerization and antibodies

L7 2462 POLYMERIZATION AND ANTIBODIES

=> s l7 and antigen

L8 671 L7 AND ANTIGEN

=> s l8 and bivalent

L9 3 L8 AND BIVALENT

=> d l9 1-3 all

L9 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2001 ACS
AN 1985:202283 CAPLUS
DN 102:202283
TI Monoclonal **antibodies** against seven sites on the head and tail of Dictyostelium myosin
AU Peltz, Gary; Spudich, James A.; Parham, Peter
CS Sch. Med., Stanford Univ., Stanford, CA, 94305, USA
SO J. Cell Biol. (1985), 100(4), 1016-23
CODEN: JCLBA3; ISSN: 0021-9525
DT Journal
LA English
CC 15-3 (Immunochemistry)
AB Ten monoclonal **antibodies** (My1-10) against D. discoideum myosin were prepd. and characterized. Nine bound to the 210-kilodalton (kD) heavy chain and 1 (My8) bound to the 18-kD light chain. They defined 6 topog. distinct antigenic sites of the heavy chain. Five binding sites (the My1, My5, My10 site, and the My2, My3, My4, and My9 sites) are located on the rod portion of the myosin mol. The position of the 6th site (the My6 and My7 site) is less certain, but it appears to be near the junction of the globular heads and the rod. Three of the **antibodies** (My2, My3, and My6) bound to myosin filaments in soln. and could be sedimented in stoichiometric amts. with the filamentous myosin. In contrast, My4, which recognized a site on the rod, inhibited the **polymn**. of monomeric myosin into filaments. A single antibody (My6) affected the actin-activated ATPase of myosin. The nature of the effect depended on the valency of the antibody and the myosin. **Bivalent** IgG and F(ab')2 fragments of My6 inhibited the actin-activated ATPase of filamentous myosin by 50% whereas univalent Fab' fragments increase the activity by 50%. The actin-activated ATPase activity of the sol. chymotryptic fragment of myosin was increased 80-90% by both (F(ab')2 and Fab' of My6.
ST monoclonal antibody Dictyostelium myosin
IT Microfilament and Microtubule
(formation of, by Dictyostelium discoideum, myosin-specific monoclonal **antibodies** inhibition of)
IT Dictyostelium discoideum
(myosin of, monoclonal **antibodies** to, formation and specificity of)
IT **Antigens**
RL: BIOL (Biological study)
(of myosin of Dictyostelium discoideum, identification and characterization of)
IT Myosins
RL: BIOL (Biological study)
(of Dictyostelium discoideum, monoclonal **antibodies** to, formation and specificity of)
IT **Antibodies**
RL: BIOL (Biological study)
(monoclonal, to myosin of Dictyostelium discoideum, formation and specificity of)
IT 9000-83-3
RL: BIOL (Biological study)
(monoclonal **antibodies** to myosin of Dictyostelium discoideum affect on)

by **bivalent antibodies** cross-linking 0.235-.mu.m polystyrene spheres coated with **antigen**. If Xn is the mole fraction of clusters contg. n spheres and X0 the mole fraction of spheres initially added, then it is found that the cluster size distributions are detd. solely by the bonding parameter b .ident. 1 - .sum.Xn/X0. The dependence of b upon the time t, the cross-linking antibody concn. [ab]0, and X0 are reported. These results were compared for b(t) and the previously reported form of the cluster size distribution Xn/X0 = (1 - b)(be-b)n-1/bn! with extant statistical and kinetic theories.

ST **antigen** antibody cluster size distribution; **polymn** kinetics model

IT **Antibodies**
RL: BIOL (Biological study)
(-**antigen** crosslinking, as cluster size distribution kinetics model)

IT Particle size
(distribution of, of **antigen**-antibody clusters, as cluster size distribution kinetics model)

IT Process simulation, biological
(of **antigen**-antibody cluster formation, as cluster size distribution kinetics model)

IT Kinetics of crosslinking
Kinetics of **polymerization**
(of **antigen**-antibody clusters, as cluster size distribution kinetics model)

IT Distribution function
(cluster, antibody-multivalent **antigen** crosslinking as model for)

L9 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2001 ACS
AN 1977:598892 CAPLUS
DN 87:198892
TI **Bivalent** affinity labeling haptens in the formation of model immune complexes
AU Plotz, Paul H.
CS Natl. Inst. Arthritis, Metab., Dig. Dis., NIH, Bethesda, Md., USA
SO Methods Enzymol. (1977), 46(Affinity Labeling), 505-8
CODEN: MENZAU
DT Journal
LA English
CC 15-1 (Immunochemistry)
Section cross-reference(s): 25

AB The synthesis and employment of bis-p-nitrophenyl esters of dicarboxylic acids for covalently linking **antibodies** directed against the p-nitrophenyl group hapten is described for the purpose of studying the phys. state of covalently-coupled **antigen**-antibody complexes. Detailed procedures are given for the prepn. of the bis-p-nitrophenyl ester of pimelic acid (I) and conditions for **polymn**. of rabbit antiserum against p-nitrophenylated bovine .gamma.-globulin with the reagent are detailed.

ST **bivalent** affinity label **antigen** antibody; immune complex **bivalent** affinity label; dinitrophenyl hapten **bivalent** affinity label

IT **Antibodies**
RL: BIOL (Biological study)
(**antigen** complexes, **bivalent** affinity labels for covalent coupling of)

IT Immunochemistry
(**bivalent** affinity labels for)

IT 49761-23-1
RL: BIOL (Biological study)
(**bivalent** affinity labeling hapten, covalent **antigen**-antibody complex formation in relation to)

=> d his

(FILE 'HOME' ENTERED AT 15:37:41 ON 19 APR 2001)

FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE, CANCERLIT' ENTERED AT 15:37:57 ON 19 APR 2001

L1 0 S (DUAL ANTIGEN BINDING SITE)

=> s (two single light chain variable regions)

L12 0 (TWO SINGLE LIGHT CHAIN VARIABLE REGIONS)

=> s (single light chain variable region)

L13 0 (SINGLE LIGHT CHAIN VARIABLE REGION)

=> s l7 and light chain?

L14 42 L7 AND LIGHT CHAIN?

=> s l8 and antigen

L15 671 L8 AND ANTIGEN

=> s l14 and l15

L16 7 L14 AND L15

=> d l16 1-7 all

L16 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2001 ACS
AN 1995:598148 CAPLUS
DN 123:81282
TI Basis for selection of improved carbohydrate-binding single-chain **antibodies** from synthetic gene libraries
AU Deng, Su-jun; MacKenzie, C. Roger; Hirama, Tomoko; Brousseau, Roland; Lowary, Todd L.; Young, N. Martin; Bundle, David R.; Narang, Saran A.
CS Inst. Biol. Sci., Natl. Res. Council Canada, Ottawa, ON, K1A 0R6, Can.
SO Proc. Natl. Acad. Sci. U. S. A. (1995), 92(11), 4992-6
CODEN: PNASA6; ISSN: 0027-8424
DT Journal
LA English
CC 15-3 (Immunochemistry)
Section cross-reference(s): 10
AB A technique is described for the simultaneous and controlled random mutation of all three heavy or **light chain** complementarity-detg. regions (CDRs) in a single-chain Fv specific for the O polysaccharide of Salmonella serogroup B. Sense oligonucleotides were synthesized such that the central bases encoding a CDR were randomized by equimolar spiking with A, G, C, and T at a level of 10% while the antisense strands contained inosine in the spiked regions. Phage display of libraries assembled from the spiked oligonucleotides by a synthetic ligase chain reaction demonstrated a bias for selection of mutants that formed dimers and higher oligomers. Kinetic analyses showed that oligomerization increased assocn. rates in addn. to slowing dissocn. rates. In combination with some contribution from reduced steric clashes with residues in heavy-chain CDR2, oligomerization resulted in functional affinities that were much higher than that of the monomeric form of the wild-type single-chain Fv.
ST Salmonella antibody Opolysaccharide mutation method library; combinatorial library method antibody functional affinity; selection improved carbohydrate binding antibody library; oligomerization functional affinity antibody combinatorial library
IT Combinatorial library
(basis for selection of improved carbohydrate-binding single-chain **antibodies** from synthetic gene libraries)
IT **Antibodies**
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(basis for selection of improved carbohydrate-binding single-chain **antibodies** from synthetic gene libraries)
IT Gene, microbial
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(libraries for synthetic; basis for selection of improved carbohydrate-binding single-chain **antibodies** from synthetic gene libraries)
IT Mutation
(method for simultaneous and controlled generation of random; basis for selection of improved carbohydrate-binding single-chain

AN 1992:5189 CAPLUS
DN 116:5189
TI Oligomeric monoclonal immunoglobulins for immunodiagnosis and therapy
IN Shuford, Walt W.; Harris, Linda J.; Raff, Howard V.
PA Bristol-Myers Squibb Co., USA
SO PCT Int. Appl., 104 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K035-14
ICS A61K039-00; A61K039-40; C12N005-02; C12N015-00
CC 15-3 (Immunochemistry)
Section cross-reference(s): 3, 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9106305	A1	19910516	WO 1990-US6426	19901106
	W: AU, CA, FI, JP, KR, NO				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
	CA 2045150	AA	19910508	CA 1990-2045150	19901106
	AU 9170303	A1	19910531	AU 1991-70303	19901106
	AU 648056	B2	19940414		
	EP 462246	A1	19911227	EP 1991-901546	19901106
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	JP 04505709	T2	19921008	JP 1991-501918	19901106
	NO 9102640	A	19910905	NO 1991-2640	19910705
PRAI	US 1989-432700	19891107			
	WO 1990-US6426	19901106			

AB Oligomeric monoclonal **antibodies** with high avidity for **antigen** are prepd. that have .gtoreq.2 Ig monomers assocd. together to form tetravalent or hexavalent Ig, esp. IgG. The oligomers are formed by substantially duplicating regions of the **light chain**, particularly the variable region. Oligomeric **antibodies** of the IgG isotype cross the placenta and can provide passive immunity to a fetus, which is particularly important for protecting newborns against, e.g. group B streptococci. A monoclonal antibody having a mol. wt. substantially greater than a typical IgG antibody was produced using V region genes cloned from the parental 4B9 lymphoblastoid cell line. The antibody (1B1 dimer) was specific for group B streptococcus, was 100-fold more active in an opsonophagocytic assay than the monomer, and passed through the placenta and into the fetus of rats. Rat pups treated with the antibody after i.p. injection of streptococci were protected at both low and high concns. of antibody. DNA sequences are shown for the 1B1 **light chain** and for chains of the 4B9 antibody.

ST oligomer monoclonal Ig diagnosis therapy; IgG oligomer Streptococcus newborn immunization; cloning IgG oligomer prodn

IT Mammal
(cell line of, oligomeric monoclonal Ig secretion by)

IT Phagocytosis
(enhancement of, with oligomeric monoclonal IgG)

IT Gene, animal
RL: PREP (Preparation)
(for Ig, cloning of, in prepn. of oligomeric monoclonal Ig for diagnosis and therapy)

IT Molecular cloning
(of genes for Ig, in prepn. of oligomeric monoclonal Ig for diagnosis and therapy)

IT **Polymerization**
(of monoclonal Ig, amino acid substitution for, in prodn. of oligomeric monoclonal Ig for immunodiagnosis and therapy)

IT Pharmaceutical dosage forms
(of oligomeric monoclonal IgG)

IT Animal cell line
(oligomeric monoclonal Ig secretion by)

IT Placenta
(oligomeric monoclonal Ig transport across, for passive immunization of fetus)

IT **Antigens**
RL: BIOL (Biological study)
(oligomeric monoclonal IgG to, prodn. of, for immunodiagnosis and therapy)

IT Plasmid and Episome

IT Animal cell line
(4B9, oligomeric monoclonal Ig derived from)
IT Immunoglobulins
RL: PREP (Preparation)
(G, monoclonal, oligomeric, prodn. of, for immunodiagnosis and therapy)
IT Immunoglobulins
RL: PREP (Preparation)
(G1, monoclonal, oligomeric, prodn. of, for immunodiagnosis and therapy)
IT Immunoglobulins
RL: PREP (Preparation)
(G2, monoclonal, oligomeric, prodn. of, for immunodiagnosis and therapy)
IT Immunoglobulins
RL: BIOL (Biological study)
(M, oligomeric monoclonal Ig derived from)
IT Embryo
(fetus, passive immunization of, with oligomeric monoclonal Ig)
IT Streptococcus
(group B, passive immunization against, in fetus and newborn, oligomeric monoclonal Ig for)
IT Therapeutics
(immuno-, oligomeric monoclonal Igs for)
IT Diagnosis
(immunol., oligomeric monoclonal Igs for)
IT Immunoglobulins
RL: PREP (Preparation)
(monoclonal, oligomeric, prodn. of, for immunodiagnosis and therapy)
IT Plasmid and Episome
(pN.gamma.1A2.1, heavy chain of oligomeric monoclonal IgG to group B streptococcus on, cloning and expression of)
IT Immunization
(passive, against streptococci, in fetus and newborn, oligomeric monoclonal Ig for)
IT 137067-93-7 137067-94-8
RL: PRP (Properties)
(amino-terminal sequence of recombinant light Ig chain of 1B1 monoclonal IgG)
IT 137748-88-0, Deoxyribonucleic acid (human clone 4B9-UK15 4B9 immunoglobulin G 1 **light chain** fragment-specifying)
137748-89-1, Deoxyribonucleic acid (human clone 4B9-UK15 immunoglobulin G 1 **light chain** fragment-specifying) 137749-00-9, Deoxyribonucleic acid (human clone pN.gamma.1A2.1 immunoglobulin G 1 heavy chain fragment-specifying) 137749-01-0, Deoxyribonucleic acid (human clone pNkA1.1 immunoglobulin G 1 **light chain** fragment-specifying)
RL: PRP (Properties)
(cloning and nucleotide sequence of)

L16 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2001 ACS
AN 1985:202283 CAPLUS
DN 102:202283
TI Monoclonal **antibodies** against seven sites on the head and tail of Dictyostelium myosin
AU Peltz, Gary; Spudich, James A.; Parham, Peter
CS Sch. Med., Stanford Univ., Stanford, CA, 94305, USA
SO J. Cell Biol. (1985), 100(4), 1016-23
CODEN: JCLBA3; ISSN: 0021-9525
DT Journal
LA English
CC 15-3 (Immunochemistry)
AB Ten monoclonal **antibodies** (My1-10) against D. discoideum myosin were prepd. and characterized. Nine bound to the 210-kilodalton (kD) heavy chain and 1 (My8) bound to the 18-kD **light chain** . They defined 6 topog. distinct antigenic sites of the heavy chain. Five binding sites (the My1, My5, My10 site, and the My2, My3, My4, and My9 sites) are located on the rod portion of the myosin mol. The position of the 6th site (the My6 and My7 site) is less certain, but it appears to be near the junction of the globular heads and the rod. Three of the **antibodies** (My2, My3, and My6) bound to myosin filaments in soln. and could be sedimented in stoichiometric amts. with the filamentous myosin. In contrast, My4, which recognized a site on the rod, inhibited the [illegible] of monomeric myosin into filaments. A single

characterization of)
IT Myosins
RL: BIOL (Biological study)
(of Dictyostelium discoideum, monoclonal **antibodies** to, formation and specificity of)
IT **Antibodies**
RL: BIOL (Biological study)
(monoclonal, to myosin of Dictyostelium discoideum, formation and specificity of)
IT 9000-83-3
RL: BIOL (Biological study)
(monoclonal **antibodies** to myosin of Dictyostelium discoideum effect on)

L16 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2001 ACS
AN 1971:138583 CAPLUS
DN 74:138583
TI Antilipoprotein autoantibodies of multiple myeloma. Comparative study of two types: IgA anti-Lp P.G. and IgG anti-Lp A.S.
AU Beaumont, Jean L.; Beaumont, Violette; Antonnucci, Micheline; Lemort, Nicole
CS Unite Rech. Atheroscler., Hop. Henri-Mondor, Creteil, Fr.
SO Ann. Biol. Clin. (Paris) (1970), 28(5), 387-99
CODEN: ABCLAI
DT Journal
LA French
CC 13 (Immunochemistry)
AB Antilipoprotein activity of the M protein (I) was studied in 3 myeloma patients with hyperlipemia (2 with IgA myeloma and 1 with IgG myeloma). I was sepd. from the circulating lipoproteins with which it was bound in vivo. The reactions of purified I with .alpha.-lipoprotein (II) and .beta.-lipoprotein (III) were studied in vitro by immunopptn., passive hemagglutination, and gel filtration. In the 2 IgA myeloma patients, I was a .gamma.1 globulin with a k **light chain** which reacted with the P.G. lipoprotein (phyllotype G for 1st patient with this disease) site common to the serum II and III of the patients and men and animals studied. III had .apprx.64 reacting sites, and II, 20. A fragment which reacted with antibody was extd. with ether and contained a phospholipid. After treatment with papain, only the Fab fragment reacted. The **antibodies** of the 2 IgA patients differed in their degree of **polymerization**. In the IgG myeloma, I was a .gamma.1 globulin with a k **light chain** which reacted with the A.S. lipoprotein (allotype S for name of patient) site, an allotype common to the patient's II and III, but found only in 3 of 50 human sera studied (in 1 all lipoprotein reacted, in the other 2 only 30). Rabbit lipoprotein did not react. There were .apprx.56 sites on III and 22 on II. The Fab fragment had 1 reacting site. In all the patients hyperlipidemia was due to the accumulation of the sol. **antigen**-antibody complexes which were cleared slowly due to direct or indirect inhibition of lipolysis. The anti-P.G. lipoprotein IgA myeloma and anti-A.S. lipoprotein IgG myeloma were models for the study of autoimmune hyperlipidemia.
ST lipoprotein antibody multiple myeloma; hyperlipemia antibody multiple myeloma
IT Globulins, immune
RL: BIOL (Biological study)
(A and G, autoantibodies to lipoproteins in, in multiple myeloma)
IT **Antibodies**
RL: BIOL (Biological study)
(auto-, to lipoproteins in myeloma)
IT Myeloma
(autoantibodies to lipoproteins in multiple, immune globulins in relation to)
IT Lipoproteins
RL: BIOL (Biological study)
(autoantibodies to, in immune glubulins in myeloma)
IT Lipids
RL: PROC (Process)
(metabolic disorders of, autoimmune hyperlipidemia)

L16 ANSWER 5 OF 7 MEDLINE
AN 2000102612 MEDLINE
DN 20102612
TI Separation of fibronectin with lysophosphatidic acid induces motility and

polymerization and myosin **light chain** phosphorylation through the activation of Rho-ROCK (Rho-kinase) cascade. When, however, the motility of MM1 cells on a glass surface was tested by phagokinetic track motility assay, LPA failed to induce the motility. Nevertheless, when the glass had been coated with fibronectin (FN), LPA could induce phagokinetic motility which was accompanied by transformation of MM1 cells to fusiform-shape and assembly of focal adhesion. beta1 integrin, the counter receptor of FN, was expressed on MM1 cells. Anti-FN antibody, anti-beta1 integrin antibody and cyclo-GRGDSPA remarkably suppressed LPA-induced phagokinetic motility. These **antibodies** suppressed LPA-induced transcellular migration through MCL, as well. These results indicate that actin **polymerization** and phosphorylation of myosin **light chain** through Rho activation are insufficient for inducing motility but the cooperative FN/beta1 integrin-mediated adhesion is necessary for both the phagokinetic motility and transcellular migration of MM1 cells.

CT Check Tags: Animal; Support, Non-U.S. Gov't
Antibodies: PD, pharmacology
Antigens, CD29: IM, immunology
Carcinoma, Hepatocellular
*Cell Movement
Cell Movement: IM, immunology
Fibronectins: IM, immunology
*Fibronectins: PD, pharmacology
Liver Neoplasms
Lysophospholipids: IM, immunology
*Lysophospholipids: PD, pharmacology
Rats
Tumor Cells, Cultured

CN 0 (**Antibodies**); 0 (**Antigens**, CD29); 0 (Fibronectins); 0 (Lysophospholipids)

L16 ANSWER 6 OF 7 MEDLINE
AN 1998215725 MEDLINE
DN 98215725
TI Rho-mediated contractility exposes a cryptic site in fibronectin and induces fibronectin matrix assembly.
AU Zhong C; Chrzanowska-Wodnicka M; Brown J; Shaub A; Belkin A M; Burridge K
CS Department of Cell Biology and Anatomy, and Lineberger Comprehensive Cancer Center, University of North Carolina, Chapel Hill, North Carolina, USA.
NC GM29860 (NIGMS)
HL45100 (NHLBI)
SO JOURNAL OF CELL BIOLOGY, (1998 Apr 20) 141 (2) 539-51.
Journal code: HMV. ISSN: 0021-9525.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199807
AB Many factors influence the assembly of fibronectin into an insoluble fibrillar extracellular matrix. Previous work demonstrated that one component in serum that promotes the assembly of fibronectin is lysophosphatidic acid (Zhang, Q., W.J. Checovich, D.M. Peters, R.M. Albrecht, and D.F. Mosher. 1994. J. Cell Biol. 127:1447-1459). Here we show that C3 transferase, an inhibitor of the low molecular weight GTP-binding protein Rho, blocks the binding of fibronectin and the 70-kD NH2-terminal fibronectin fragment to cells and blocks the assembly of fibronectin into matrix induced by serum or lysophosphatidic acid. Microinjection of recombinant, constitutively active Rho into quiescent Swiss 3T3 cells promotes fibronectin matrix assembly by the injected cells. Investigating the mechanism by which Rho promotes fibronectin **polymerization**, we have used C3 to determine whether integrin activation is involved. Under conditions where C3 decreases fibronectin assembly we have only detected small changes in the state of integrin activation. However, several inhibitors of cellular contractility, that differ in their mode of action, inhibit cell binding of fibronectin and the 70-kD NH2-terminal fibronectin fragment, decrease fibronectin incorporation into the deoxycholate insoluble matrix, and prevent fibronectin's assembly into fibrils on the cell surface. Because Rho stimulates contractility, these results suggest that Rho-mediated contractility promotes assembly of fibronectin into a fibrillar matrix. One mechanism by which contractility could enhance fibronectin assembly is

CT Check Tags: Animal; Support, U.S. Gov't, P.H.S.
Antigens, CD29: ME, metabolism
Azepines: PD, pharmacology
Blood
Breast: CY, cytology
Cell Line, Transformed
Diacetyl: AA, analogs & derivatives
Diacetyl: PD, pharmacology
Enzyme Inhibitors: PD, pharmacology
Epithelial Cells
Epitopes
*Extracellular Matrix: ME, metabolism
Fibronectins: BI, biosynthesis
*Fibronectins: ME, metabolism
GTP-Binding Proteins: AI, antagonists & inhibitors
*GTP-Binding Proteins: PH, physiology
Lysophospholipids: PD, pharmacology
Mice
Microfilaments
Microinjections
Myosin-Light-Chain Kinase: AI, antagonists & inhibitors
Naphthalenes: PD, pharmacology
NAD(P)(+)-Arginine ADP-Ribosyltransferase: PD, pharmacology
Recombinant Fusion Proteins
Stress, Mechanical
3T3 Cells
RN 109376-83-2 (ML 7); 431-03-8 (Diacetyl); 57-71-6 (diacetylmonoxime)
CN EC 2.4.2.- (exoenzyme C3, Clostridium botulinum); EC 2.4.2.31 (NAD(P)(+)-Arginine ADP-Ribosyltransferase); EC 2.7.1.117 (Myosin-**Light-Chain** Kinase); EC 3.6.1.- (rhoA GTP-Binding Protein); EC 3.6.1.- (GTP-Binding Proteins); 0 (**Antigens**, CD29); 0 (Azepines); 0 (Enzyme Inhibitors); 0 (Epitopes); 0 (Fibronectins); 0 (Lysophospholipids); 0 (Naphthalenes); 0 (Recombinant Fusion Proteins)

L16 ANSWER 7 OF 7 CANCERLIT
AN 2000102612 CANCERLIT
DN 20102612
TI Cooperation of fibronectin with lysophosphatidic acid induces motility and transcellular migration of rat ascites hepatoma cells.
AU Ayaki M; Mukai M; Imamura F; Iwasaki T; Mammoto T; Shinkai K; Nakamura H; Akedo H
CS Department of Tumor Biochemistry, Osaka Medical Center for Cancer and Cardiovascular Diseases, 3-3 Nakamichi 1-chome, Higashinari-ku, 537-8511, Osaka, Japan. ayaki@mail.mc.pref.osaka.jp
SO BIOCHIMICA ET BIOPHYSICA ACTA, (2000). Vol. 1495, No. 1, pp. 40-50. Journal code: A0W. ISSN: 0006-3002.
DT Journal; Article; (JOURNAL ARTICLE)
FS MEDL; L; Priority Journals; Cancer Journals
LA English
OS MEDLINE 20102612
EM 200007
AB We have previously shown that the transcellular migration of rat ascites hepatoma (AH130-MM1) cells through a cultured mesothelial cell monolayer (MCL) is triggered with lysophosphatidic acid (LPA) that stimulates actin **polymerization** and myosin **light chain** phosphorylation through the activation of Rho-ROCK (Rho-kinase) cascade. When, however, the motility of MM1 cells on a glass surface was tested by phagokinetic track motility assay, LPA failed to induce the motility. Nevertheless, when the glass had been coated with fibronectin (FN), LPA could induce phagokinetic motility which was accompanied by transformation of MM1 cells to fusiform-shape and assembly of focal adhesion. beta1 integrin, the counter receptor of FN, was expressed on MM1 cells. Anti-FN antibody, anti-beta1 integrin antibody and cyclo-GRGDSPA remarkably suppressed LPA-induced phagokinetic motility. These **antibodies** suppressed LPA-induced transcellular migration through MCL, as well. These results indicate that actin **polymerization** and phosphorylation of myosin **light chain** through Rho activation are insufficient for inducing motility but the cooperative FN/beta1 integrin-mediated adhesion is necessary for both the phagokinetic motility and transcellular migration of MM1 cells.
CT Check Tags: Animal; Support, Non-U.S. Gov't
Antibodies: PD, pharmacology
[illegible]: CD29; IM, immunology

(FILE 'HOME' ENTERED AT 15:37:41 ON 19 APR 2001)

FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE, CANCERLIT' ENTERED AT 15:37:57 ON 19 APR 2001

L1	0	S	(DUAL ANTIGEN BINDING SITE)
L2	1544355	S	ANTIGEN
L3	384	S	L2 AND JUXTAPOSED
L4	240	S	L3 AND GENE?
L5	0	S	L4 AND DIMER
L6	1	S	L4 AND DIMER?
L7	2462	S	POLYMERIZATION AND ANTIBODIES
L8	671	S	L7 AND ANTIGEN
L9	3	S	L8 AND BIVALENT
L10	3	S	L8 AND BIVALENT?
L11	0	S	JANUSBODIES?
L12	0	S	(TWO SINGLE LIGHT CHAIN VARIABLE REGIONS)
L13	0	S	(SINGLE LIGHT CHAIN VARIABLE REGION)
L14	42	S	L7 AND LIGHT CHAIN?
L15	671	S	L8 AND ANTIGEN
L16	7	S	L14 AND L15

WEST

Generate Collection

L2: Entry 16 of 18 File: USPT Oct 14, 1986

DOCUMENT-IDENTIFIER: US 4617262 A
TITLE: Assaying for circulating immune complexes with labeled protein A

CLPR:
2. The method of claim 1 wherein steps a) and b) are conducted simultaneously by contacting said serum with a solution containing labeled SPA and polyethylene glycol.

CLPR:
13. The method of claim 12 wherein steps a) and b) are conducted simultaneously by contacting said serum with a solution containing enzyme-labeled SPA and polyethylene glycol.

CLPV:
(a) contacting said circulating immune complexes in solution in said serum with a staphylococcal protein-A(SPA) linked to a detectable label, whereby a CIC-protein-A-label complex is formed,

CLPV:
(b) selectively precipitating said CIC-SPA-label complex by contacting the complex with polyethylene glycol,

CLPV:
(c) separating said precipitated CIC-SPA-label complex from said serum,

CLPV:
(a) contacting said circulating immune complexes in solution in said serum with staphylococcal protein-A (SPA) linked to an enzyme, whereby a CIC-protein-A-enzyme complex is formed,

CLPV:
(b) selectively precipitating said CIC-SPA-enzyme complex by contacting the complex with polyethylene glycol,

CLPV:
(c) separating the precipitated CIC-SPA-enzyme complex from said serum,

WEST

Generate Collection

L11: Entry 16 of 60 File: USPT Dec 21, 1999

US-PAT-NO: 6004811
DOCUMENT-IDENTIFIER: US 6004811 A

TITLE: Redirection of cellular immunity by protein tyrosine kinase chimeras

DATE-ISSUED: December 21, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Seed; Brian	Boston	MA	N/A	N/A
Romeo; Charles	Belmont	MA	N/A	N/A
Kolanus; Waldemar	Watertown	MA	N/A	N/A

US-CL-CURRENT: 435/372.3; 435/375, 435/6, 435/69.1, 536/23.4, 536/23.5

CLAIMS:

We claim:
1. An isolated cytotoxic T-cell which expresses a membrane-bound chimeric receptor, said chimeric receptor comprising: (a) an intracellular portion of a Syk protein-tyrosine kinase which signals said cytotoxic T-cell to destroy a receptor-bound target cell; (b) a transmembrane domain; and (c) an extracellular portion of an immunoglobulin superfamily protein which specifically recognizes and binds said target cell; and wherein said chimeric receptor signals said cytotoxic T-cell to destroy said target cell.
2. The cytotoxic T cell of claim 1, wherein said intracellular portion includes human Syk amino acids 336-628 g or porcine Syk amino acids 338-630.
3. The cytotoxic T-cell of claim 1, wherein said target cell is infected with an immunodeficiency virus.
4. The cytotoxic T-cell of claim 3, wherein said extracellular portion comprises an HIV envelope-binding portion of CD4.
5. An isolated cytotoxic T-cell which expresses at least two different membrane-bound chimeric receptors,
the first of said chimeric receptors comprising: (a) an intracellular portion of a ZAP-70 protein tyrosine-kinase; (b) a transmembrane domain; and (c) an extracellular portion of an immunoglobulin superfamily protein which specifically recognizes and binds a target cell; and
the second of said chimeric receptors comprising (a) an intracellular portion of a Src family protein-tyrosine kinase; (b) a transmembrane domain; and (c) an extracellular portion of an immunoglobulin superfamily protein which specifically recognizes and binds said target cell; and
wherein said ZAP-70 and said Src family protein-tyrosine kinases together signal said cytotoxic T-cell to destroy said target cell when said extracellular portions of said first and said second chimeric receptors are bound to said target cell.
6. The cytotoxic T-cell of claim 5, wherein said Src family protein-tyrosine kinase is Fyn.
7. The cytotoxic T-cell of claim 5, wherein said Src family protein-tyrosine kinase is Lck.
8. The cytotoxic T cell of claim 5, wherein said ZAP-70 portion includes human ZAP-70 Tyr 369.
9. The cytotoxic T-cell of claim 5, wherein said target cell is infected with an immunodeficiency virus.
10. The cytotoxic T cell of claim 9, wherein at least one said extracellular portion comprises an HIV envelope-binding portion of CD4.
11. The cytotoxic T-cell of claims 1 or 5, wherein said signaling is

MHC-independent.
12. The cytotoxic T cell of claims 1 or 5, wherein said extracellular portion comprises the ligand-binding portion of a receptor, the receptor-binding portion of a ligand, or the antigen-binding portion of an antibody.
13. DNA encoding a chimeric receptor which comprises (a) an intracellular portion of a Syk protein-tyrosine kinase; (b) a transmembrane domain; and (c) an extracellular portion of an immunoglobulin superfamily protein.
14. A vector comprising the DNA of claim 13.
15. The DNA of claim 13, wherein said intracellular portion includes human Syk amino acids 336-628 or porcine Syk amino acids 338-630.
16. The DNA of claim 13, wherein said extracellular portion comprises an HIV-envelope binding portion of CD4.
17. The DNA of claim 13, wherein said extracellular portion comprises the ligand-binding portion of a receptor, the receptor-binding portion of a ligand, or the antigen-binding portion of an antibody.
18. The cytotoxic T cell of claim 1, wherein said Syk protein-tyrosine kinase is a human Syk protein-tyrosine kinase.
19. The cytotoxic T cell of claim 5, wherein said ZAP-70 protein-tyrosine kinase is a human ZAP-70 protein-tyrosine kinase.
20. The cytotoxic T cell of claim 5, wherein said Src protein-tyrosine kinase is a human Src protein-tyrosine kinase.
21. The cytotoxic T cell of claims 1 or 5, wherein said immunoglobulin superfamily protein is CD16.
22. The DNA of claim 13, wherein said Syk protein-tyrosine kinase is a human Syk protein-tyrosine kinase.
23. The DNA of claim 13, wherein said immunoglobulin superfamily protein is CD16.